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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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09/713,017

11/16/2000

Andre Choulika

02356.0077-01

6042

22852

7590

06/05/2006

EXAMINER

EPFS FORD, JANET L

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901 NEW YORK AVENUE, NW
WASHINGTON, DC 20001-4413

ART UNIT

PAPER NUMBER

1633

DATE MAILED: 06/05/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/713,017

Applicant(s)

CHOULIKA ET AL.

Examiner

Janet L. Epps-Ford

Art Unit

1633

– The MAILING DATE of this communication appears on the cover sheet with the correspondence address –

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 10 May 2006.
- 2a) ☐ This action is FINAL. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 39 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 39 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|---|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

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Response to Amendment

1. Applicant's request for reconsideration of the finality of the rejection of the last Office action is persuasive and, therefore, the finality of that action is withdrawn.
2. The indicated allowability of claim 39 set forth in the prior Office Action is withdrawn for the reasons set forth below.

Claim Rejections - 35 USC § 112

3. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

4. Claim 39 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 39, lines 1-4 recites "a nucleic acid molecule comprising retroelements that comprise a recombinant provirus when a target cell is infected by a retrovirus containing said retroelements; said retroelements comprise a 3' and/or 5' LTR region...." This phrase is vague and indefinite since it is clear from line 1 that the claimed nucleic acid molecule comprises "retroelements," and not a retroelement, and furthermore, it is clear from the specification (see page 3, 2nd paragraph), and the state of the art, that formation of a provirus by means of a retrovirus, requires both a 3' and 5' LTR sequence.

Moreover, claim 39 is indefinite since it is not readily apparent that the claim is directed merely to the "nucleic acid molecule" as recited in lines 1-11 of claim 1, or to

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the plasmid deposited under CNCM Accession No. I-1599, further comprising said nucleic acid molecule. Moreover, it is unclear if the description of the nucleic acid molecule recited in lines 1-11 of claim 1, actually represents the structural characteristics of the plasmid deposited under CNCM Accession No. I-1599.

Claim Rejections - 35 USC § 103

5. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

6. Claim 39 is rejected under 35 U.S.C. 103(a) as being unpatentable over Gilboa et al. (WO 89/11539 A1) in view of Enquist et al. (EP300422A2), and Anderson (US Patent No. 5,629,159).

The prior art is applied to the extent that claim 39 reads on "a nucleic acid molecule comprising retroelements that comprise a recombinant provirus when a target cell is infected by a retrovirus containing said retroelements; said retroelements comprise a 3' and/or 5' LTR region; said insertion sequence comprises a nucleotide sequence of interest, which can be expressed in the target cell and which can be transferred with said retroelements into the target cell and integrated into the recombinant provirus and a recombinase recognition site for the elimination of proviral sequences in the recombinant provirus, which are not necessary for the expression of the nucleotide sequence of interest in the target cell after integration of the recombinant provirus into the target cell."

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Gilboa et al. describe the double copy retroviral vector, which comprises an insertion of the ADA gene sequence into the U3 region of a 3' LTR, see for example Figure 4, and page 13, lines 12-29. Additionally, Gilboa et al. generically describes: a retroviral vector for introducing into a eukaryotic cell DNA encoding a transcription unit which comprises a first DNA sequence which is the reverse transcript of at least a portion of a retrovirus, said portion including both the 5' LTR sequence and the 3' LTR sequence of the retrovirus, and a second DNA sequence encoding the transcription unit which is inserted into the U3 region of the 3' LTR sequence. Gilboa et al. further teach that the second DNA sequence of the retroviral vector encoding encodes an RNA molecule, wherein the RNA encodes a recognition sequence for a DNA or RNA binding protein (see pages 46-47, claims 1, 10 and 12 of the Gilboa et al. WIPO document). Gilboa et al. does not teach wherein the recognition sequence is a recombinase recognition sequence, wherein the retroviral vector encodes a recombinase protein, or wherein the nucleotide sequence of interest is an antisense RNA or a ribozyme sequence.

Enquist discloses the desirability of using recombination as a means of modifying retroviral vectors (page 5, lines 43-57 and page 7, lines 26-39). A viral vector is modified by the insertion of loxP elements (page 5, lines 1-26) and the loxP element so included is a recognition sequence for the bacteriophage P1 Cre recombinase, which is disclosed as either inserting sequences into the viral vector, and/or removing sequences from the vector (page 9, lines 1-5). The sequence of interest may encode a

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polypeptide. Enquist et al. does not disclose such a viral vector wherein the Cre recombinase is encoded within the vector itself.

Anderson discloses retroviral vector constructions (see figures 1a-1d and 2a-b) which contain LTR elements that express sequences of interest that are integrated into a cis-acting region of the virus, encodes selectable markers, and which has promoters and other control elements. Such vectors were modified to contain loxP elements (fig. 2a-2b) for the removal of an intervening nucleotide sequence. The use of the Cre/loxP and FLP/FRT recombinase systems is disclosed (col. 7, lines 20-28) and the gene encoding the recombinase (either Cre or FLP) is part of the retroviral construct (col. 8, lines 38-56). The desirability of removing or eliminating the recombinase by the recombination event, along with a sequence of interest, is further disclosed at col. 8, lines 47-52. At column 11, lines 41-67, the use of replication defective retroviral vectors is described in detail, along with methods of using the vectors.

It would have been obvious to one of ordinary skill in the art at the time of the instant invention to combine the teachings of Gilboa et al. in view of Enquist et al., and Anderson to make the instant invention. In seeking alternative means to express a protein using retroviral vectors, one of skill in the art would have combined the teachings of Gilboa et al. with regards to replication deficient retroviral vectors with the teachings of Enquist et al. with regard to the utility of recombination as a means of preparing and modifying vectors of all types, including retroviral vectors, for the known and expected property of effective insertion or removal of a sequence of interest into or from the vector. Additionally, one of ordinary skill in the art at the time of the instant

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invention would have been motivated to introduce recombinase recognition sites into the LTR regions of the vectors of Gilboa et al. since Gilboa et al. expressly contemplates the introduction of recognition sites for DNA or RNA binding proteins, and Enquist et al. describe the introduction of the 34 base pair recognition site (lox site) for the DNA binding protein, Cre recombinase. Furthermore, one of ordinary skill in the art at the time of the instant invention would have been motivated to further combine the teachings of Anderson with regard to encoding the recombinase directly on the retroviral vector, for the known and expected property disclosed by Anderson, namely for the simultaneous removal of the recombinase enzyme along with the sequence of interest. In so doing, one of skill in the art would have prepared a recombinant vector that would integrate into the genome, wherein one could then induce the (column 8, lines 38/55) removal sequences integrated into the genome by the retroviral vector, along with the recombinase. Given the teachings of the prior art and the knowledge of one of ordinary skill in the art, it must be considered that the ordinary skilled artisan would have had a reasonable expectation of success in practicing the claimed invention. Thus, the invention as a whole would have been *prima facie* obvious at the time the instant invention was made.

Double Patenting

7. Claim 39 is provisionally rejected under 35 U.S.C. 101 as claiming the same invention as that of claim 39 of copending Application No. 11/431,075. This is a provisional double patenting rejection since the conflicting claims have not in fact been patented.

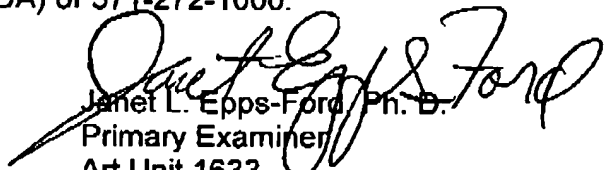
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8. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Janet L. Epps-Ford whose telephone number is 571-272-0757. The examiner can normally be reached on M-F, 10:00 AM through 6:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dave T. Nguyen can be reached on 517-272-0731. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.



Janet L. Epps-Ford, Ph. D.
Primary Examiner
Art Unit 1633

JLE